

# Clinical Outcomes of Repeat Ketamine Treatment for Treatment Resistant Depression

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## INTRODUCTION

- It is estimated that as many as 1 in 3 patients with major depressive disorder will not respond to current treatment approaches, resulting in high prevalence of treatment resistant depression (TRD) in Canada.<sup>1</sup>
- Patients with TRD report longer depressive episodes, polypharmacy use, more medication side effects, higher rates of disability and higher direct and indirect healthcare costs.<sup>1,2</sup>
- Numerous clinical trials have shown that sub-anesthetic doses of intravenous (IV) and intranasal (IN) ketamine produce rapid antidepressant effects that last up to 20 days or longer among patients with TRD.
- While there is an interest in translating clinical trial protocols into long-term treatment models to maintain therapeutic benefits, few studies have examined clinical outcomes of long-term ketamine treatment.
- Therefore, we conducted a retrospective chart review to examine clinical outcomes in a large case series of patients with TRD who attended a local ketamine clinic at Victoria Hospital in Prince Albert, Saskatchewan.

## METHODS

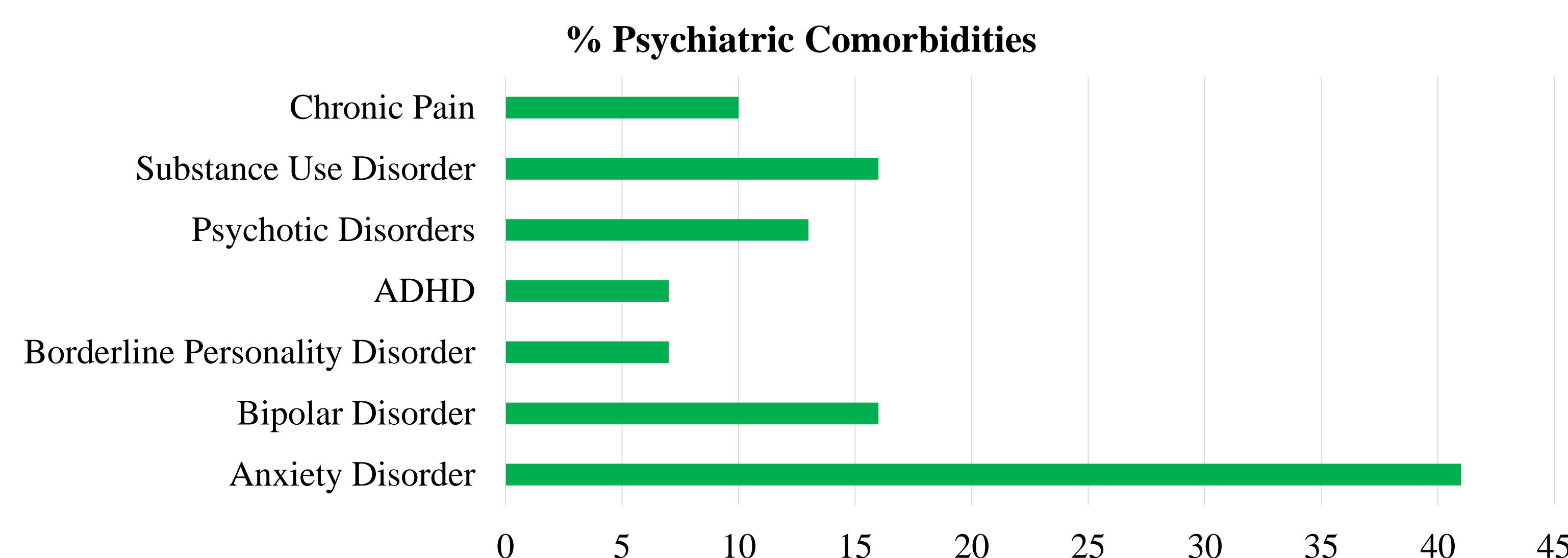
- A waiver of consent was obtained and ethical and operational approvals were obtained from the SHA Research Ethics Board.
- All patients (n = 92) who were diagnosed with TRD during clinical assessment and who received more than six ketamine infusion at the clinic between June 2016 and October 2019 were included in the review.
- Demographic information, clinical characteristics, Hamilton Depression Rating Scale (HAM-D) scores, clinical notes and adverse side effects were extracted from patient charts.
- Short-term induction ketamine treatment was defined as the first 6 ketamine treatments and long-term maintenance ketamine treatment was defined as more than 6 treatment sessions.
- Clinical improvement during induction was defined as a  $\geq 50\%$  reduction in HAM-D scores compared to baseline. Sustained clinical improvement during maintenance was defined by a lack of return to baseline scores.
- Chart information was entered and coded in SPSS and descriptive statistics were used to summarize information.



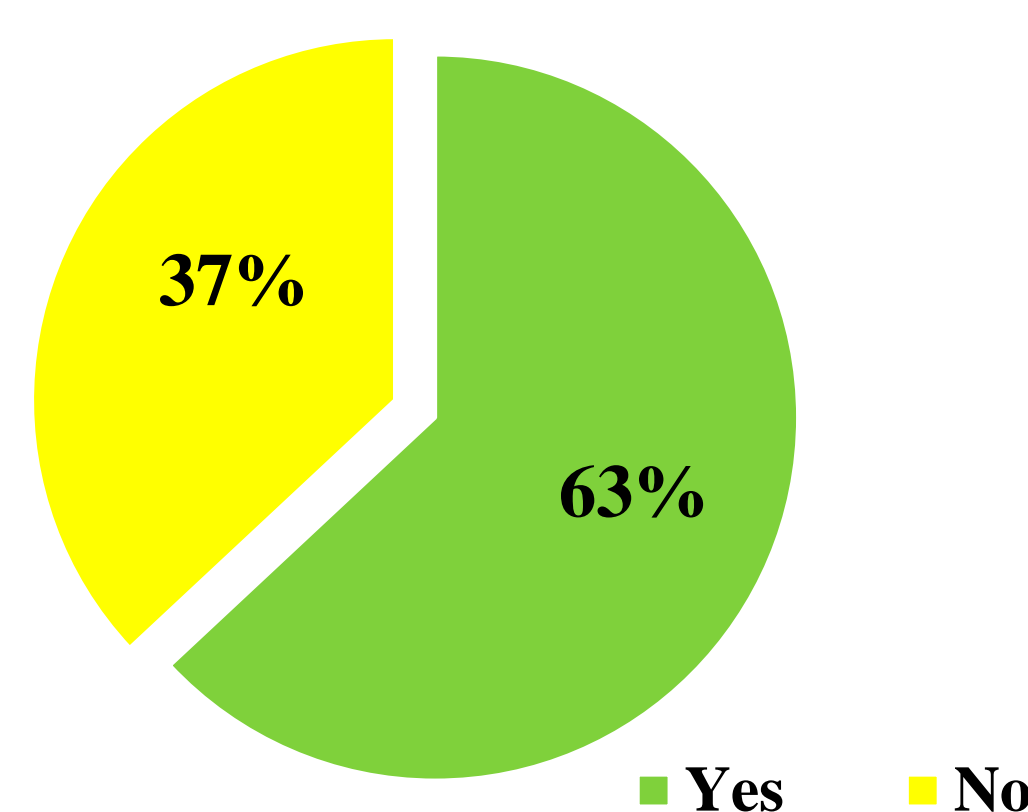
## RESULTS

### Patient Characteristics (n = 92)

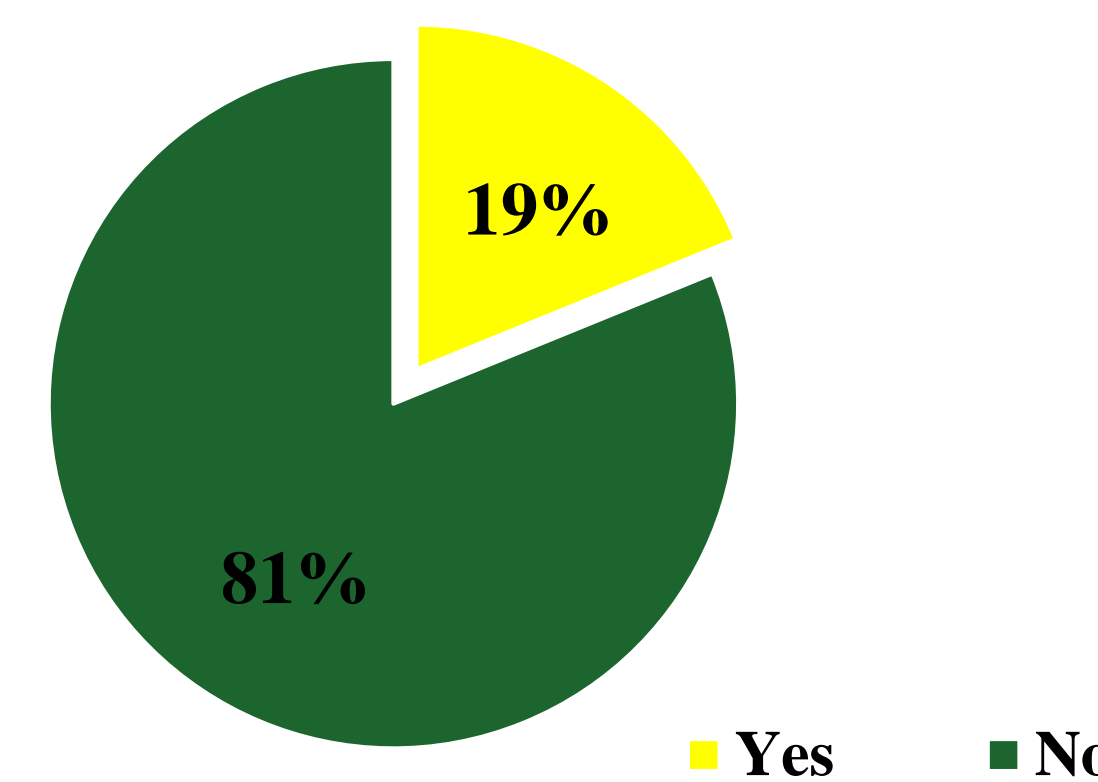
- In total, 92 patient charts met the criteria for inclusion
- Patients ranged in age from 14 to 77 (mean age = 43±16) with 66 (61%) being female.
- In total 65 (71%) reported other comorbid psychiatric disorders and 56 (61%) reported suicidal thoughts or behaviors upon presenting to the clinic.
- The duration of treatment ranged from 6 to 218 weeks (mean number of weeks = 73±50 weeks) and the number of treatments ranged from 7 to 100 (mean number of treatments = 23±16 treatments).



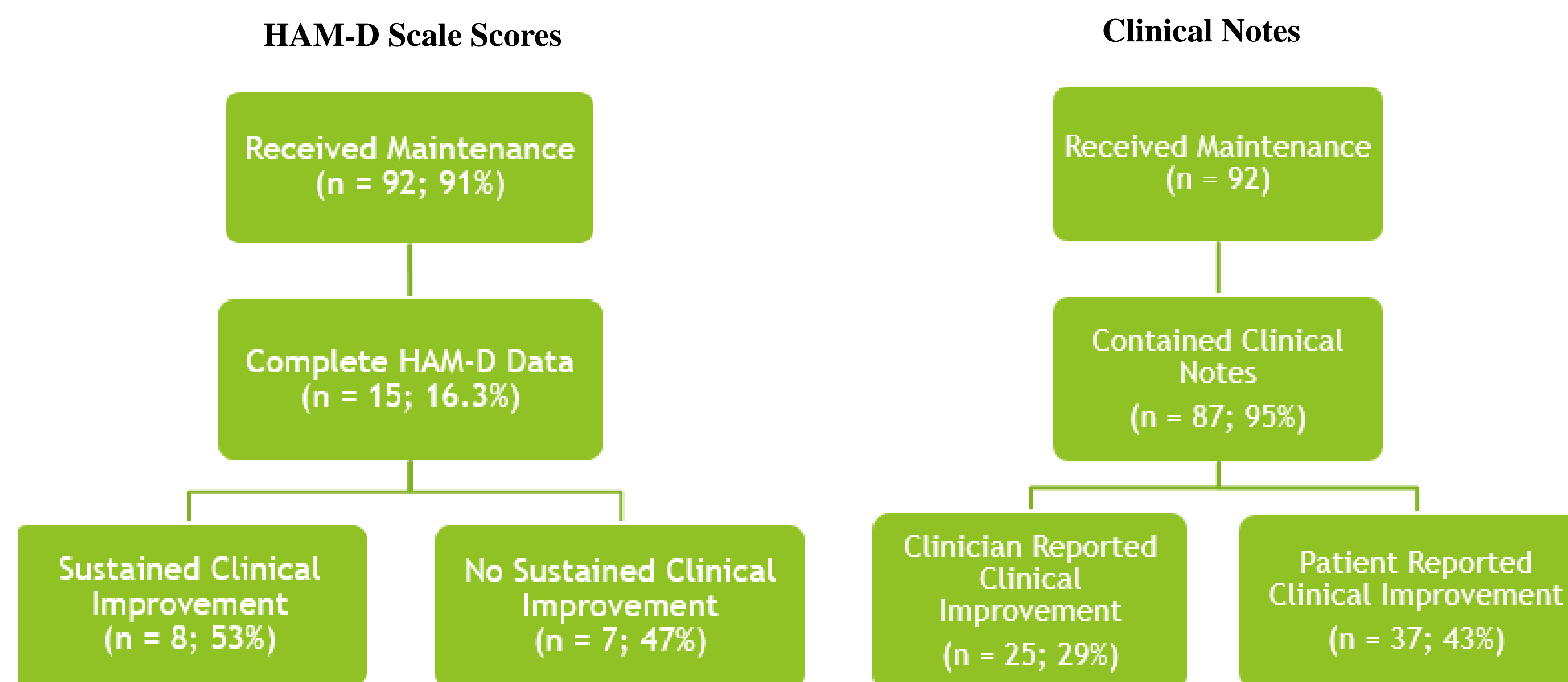
### Previous Psychiatric Hospitalization



### Concurrent Psychotherapy

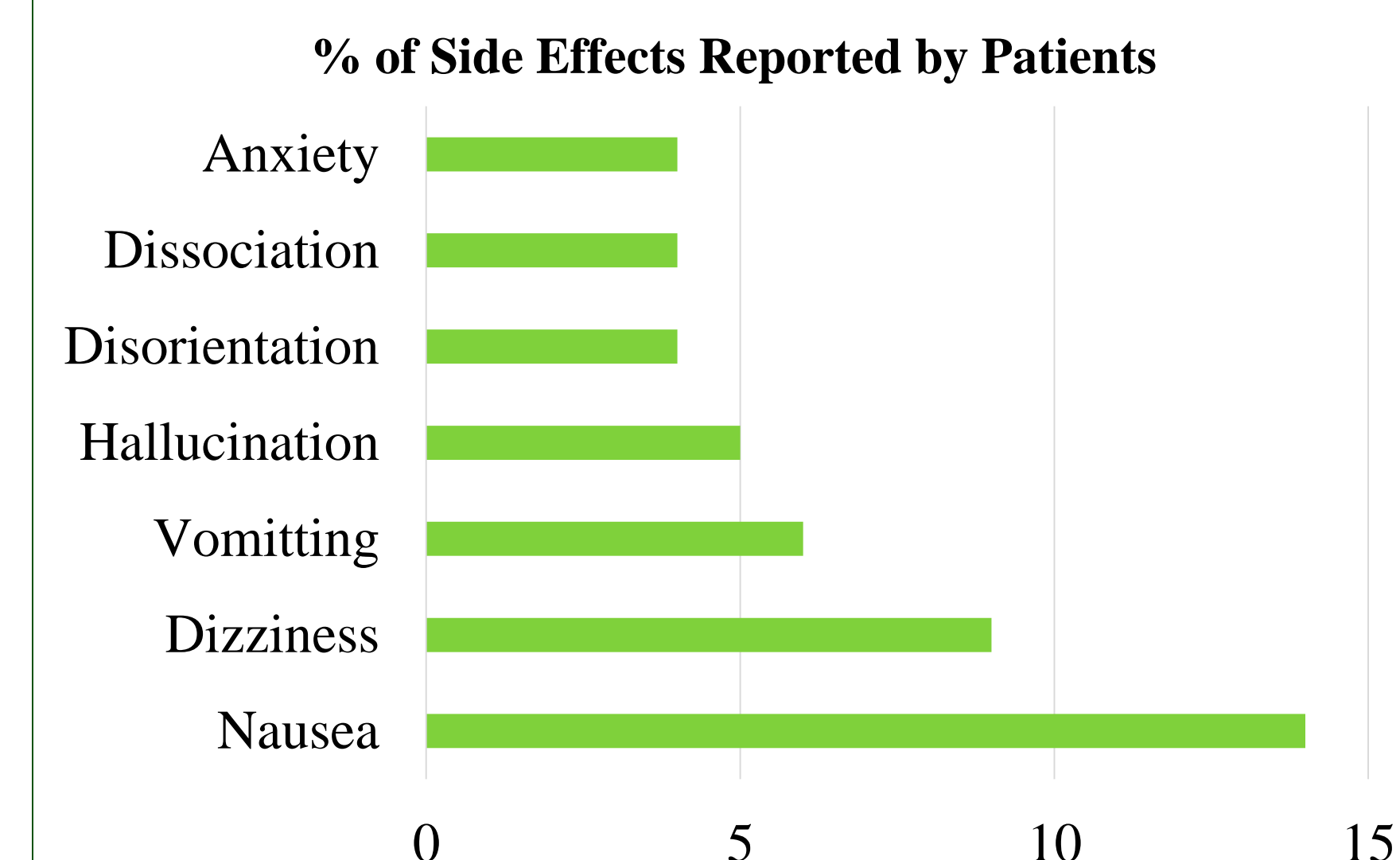


### Clinical Outcomes During Long-Term Maintenance Treatment



- Complete HAM-D scale scores were only complete for 15 (16%) of patient charts.
- Of these 15 charts, 8 (53.3%) maintained clinical improvements throughout the course of maintenance treatment.
- Clinical notes were only available for 87 (95%) of patient charts.
- Of these 87 charts, 25 (27%) included clinical reports of clinical improvement and 37 (40%) included patient or family reports of clinical improvement.

### Adverse Side Effects



- Overall 80 (58%) of patients reported no side effects associated with their ketamine treatment

## DISCUSSION

- Overall, ketamine was well tolerated among patients undergoing long-term maintenance ketamine treatment. There were no serious side effects and minor side effects were transient and resolved before discharge.
- Patients remained engaged in ketamine treatment for extended periods and across a high number of treatments which may suggest that patients perceived ketamine treatment to be beneficial.
- Findings suggest that in between 25-50% of patients experience some benefit of long-term maintenance ketamine treatment.
- Less than 1 in 5 patients reported attending psychological services, which suggests that there is a need for improved access to and utilization of psychological services among patients with TRD.

## LIMITATIONS

- Information was limited to what was documented in patient charts and documentation practices varied across patient charts.
- Patients often completed the HAM-D scale on their own rather than through consultation with a care provider.
- There was marked variability in the frequency and dosage of IV ketamine treatments.
- No design or statistical analyses were used to control for confounding factors.

## CONCLUSION

- Long-term maintenance ketamine may be a promising treatment for patients living with TRD; however, more research is needed to determine the characteristics of patients who respond favorably.
- Future research is also needed to identify any potential health risks associated with long-term ketamine treatment to determine which patients ketamine treatment is not a suitable treatment option.

## REFERENCES

- Rizvi, A. J., Trivedi, M. H., Wisniewski et al. (2014). Treatment-resistant depression in primary care across Canada. *The Canadian Journal of Psychiatry*, 59(7), 359-357.
- Ivanova, J.I., Birbaum, H. G., Kidolezi, Y., et al. (2010). Direct and indirect costs of employees with treatment resistant and non-treatment resistant major depressive disorder. *Current medical research and opinion*, 26(10), 2475-2484.